## REMARKS

Claims 1, 3 – 4, 6 – 10, and 18 are currently pending. Claims 1, 7, and 18 are the pending independent claims. In the Office Action, dependent Claim 5 was objected to as failing to further limit the subject matter of the previous claim. On the merits, Claims 1 – 10, 18, and 19 were rejected under Section 103 as allegedly obvious over PCT publication WO 2004/066997 to Antoncic et al. in combination with a WHO Drug Information publication, the Maggi reference, and U.S. Patent Publication No. US 2006/0177498 to Bharatrajan et al. ("Bharatrajan").

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. Objection to Claim 5.

In response to the objection that dependent Claim 5 fails to further limit the subject matter of Claim 1, from which it depends, Applicants have herein cancelled Claim 5. Accordingly this objection is now moot.

II. Prior Art Rejections.

The Examiner contends that the subject matter of Claims 1 – 10, 18, and 19 would have been obvious to a person of ordinary skill from Antoncic combined with the WHO Drug Information publication, the Maggi reference, and Bharatrajan. It is respectfully submitted that this obviousness rejection is not well taken and cannot be lawfully maintained for two main reasons, as explained below. One reason is that the Examiner has failed to put forward evidence sufficient to show that a person of ordinary skill would have had any motivation or incentive to combine the teachings of these references relied in the manner proposed by the Examiner. In the absence of such evidence, it can only be assumed that the Examiner simply used Applicants' claims like a grocery list and "shopped" the prior art in an effort to find all the requirements of the claims.

Second, even if there was sufficient evidence as to why a person of ordinary skill, with no knowledge of Applicants' claimed invention, would have combined these references in the manner imagined by the Examiner, and there is no such evidence, the fact remains that the requirements called for in Applicants' claims are not shown in the combination assembled by the Examiner.

Independent Claim 1 recites a pharmaceutical composition comprising a tablet core, wherein the tablet core comprises, among other things: (1) a potassium salt of losartan which exists in a first polymorph form susceptible to interconversion into one or more other polymorph forms, (2) from about 50% to about 70% by weight silicified microcrystalline cellulose, and (3) from about 1 % to about 10 % by weight of a stabilizing substance selected from the group consisting of colloidal silicon dioxide, finely divided silicon dioxide, magnesium oxide, calcium oxide, and polyethylene glycol. Similarly, independent Claim 18 recites a method for treating hypertension and/or chronic renal failure comprising administering to a patient in need thereof a pharmaceutical composition along the lines of that recited in Claim 1.

This unique combination of ingredients is shown to limit undesired interconversion of losartan to these other polymorph forms. The results of Example 1 are nothing short of remarkable. A composition of the potassium salt of losartan together with anhydrous colloidal silicon dioxide and PEG600 according to one embodiment of the claimed invention was shown to almost totally suppress interconversion under relatively severe conditions, with very little observed change in the crystallinity compared to compositions according to the prior art, which completely converted into other forms.

Nothing in the prior art would have suggested this to a person of ordinary skill. It is completely unexpected.

Antoncic is said to be the primary reference; however, the Examiner can see that Antoncic does not teach the inclusion of from about 1 % to about 10 % by weight of a stabilizing substance selected from the group consisting of colloidal silicon dioxide, finely divided silicon dioxide, magnesium oxide, calcium oxide, and polyethylene glycol in his composition. For this, the Examiner turns to Bharatrajan, from which he attempts to transplant this limitation into Antoncic.[1]

However, Bharatrajan does not, under the law of "obviousness," supply the disclosure missing in Antoncic. The reason is simple. Bharatrajan is not directed to pharmaceutical compositions comprising losartan or potassium salts of losartan. Rather, Bharatrajan focuses on

[1] It is the Applicants' understanding that the WHO Drug Information publication and the Maggi reference are cited only in regard to the identify of various trade names and common names used for anhydrous silicon dioxide and not in regard to the weight percentage specified in the claims. Thus these two references add nothing to the disclosures of Antoncic and Bharatrajan beyond these trade and common names.

compositions of ramipril, an entirely different class of pharmaceutical. Ramipril has an entirely different chemical structure. It presents its own unique issues that are not shown to bear any relation to the interconversion/ stability issues of the losartan compounds of the present invention. Moreover, the excipients described by Bharatrajan are used to prevent reactive degradation of ramipril into its "diacid form" or into the "cyclized form" ramipril diketopiperzide. *See* Bharatrajan, page 1, ¶ 5. *Bharatrajan teaches nothing about how one could present polymorphic interconversion* of pharmaceutical active ingredients that are susceptible to such interconversions, such as a potassium salt of losartan.

This is very apparent. It has not been shown why a person of ordinary skill would have any motivation or incentive whatsoever to look to Bharatrajan for a solution to the problem of polymorphic interconversion. As a result, these references would not have been "obviously" combinable in the first place. But even if some reason had been shown as to why a person of skill working on the problem of polymorphic interconversion would consider the disclosure of Bharatrajan, and it has not been, the result would still be a complete void insofar as any teaching as to how one might go about solving this problem. There is no meaningful relationship of Antoncic and Bharatrajan in relation to the problem Applicants were working on, and no objective consideration of the two references without any knowledge of Applicants' invention would have suggested the solution embodied in the Applicants' claims.

Thus, the teachings of Bharatrajan are simply unrelated to the issues facing Applicants in the present situation and no reason has been shown as to why a person of ordinary skill would look to Bharatrajan's teaching about the use of material to help avoid reactive degradation of ramipril when contemplating ways to control polymorphic interconversion of a material such as losartan. He or she simply would not have looked to the Bharatrajan reference for any idea of what to do to address the entirely different problem with losartan; but even if a person of ordinary skill did somehow happen to run across Bharatrajan in his search for idea for dealing with the losartan polymorphic interconversion problem, NOTHING in Bharatrajan would have led him/her to the solution embodied in Applicants' claims. This much is evident beyond any doubt! Thus, the obviousness rejections of Claims 1 and 18 (and their dependent claims) based on Antoncic combined with Bharatrajan is without any merit, and cannot reasonably be maintained.

In light of the foregoing, Applicants urge the Examiner to reconsider the application, to withdraw the rejections, and to issue a notice of allowance at the earliest possible convenience.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,

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